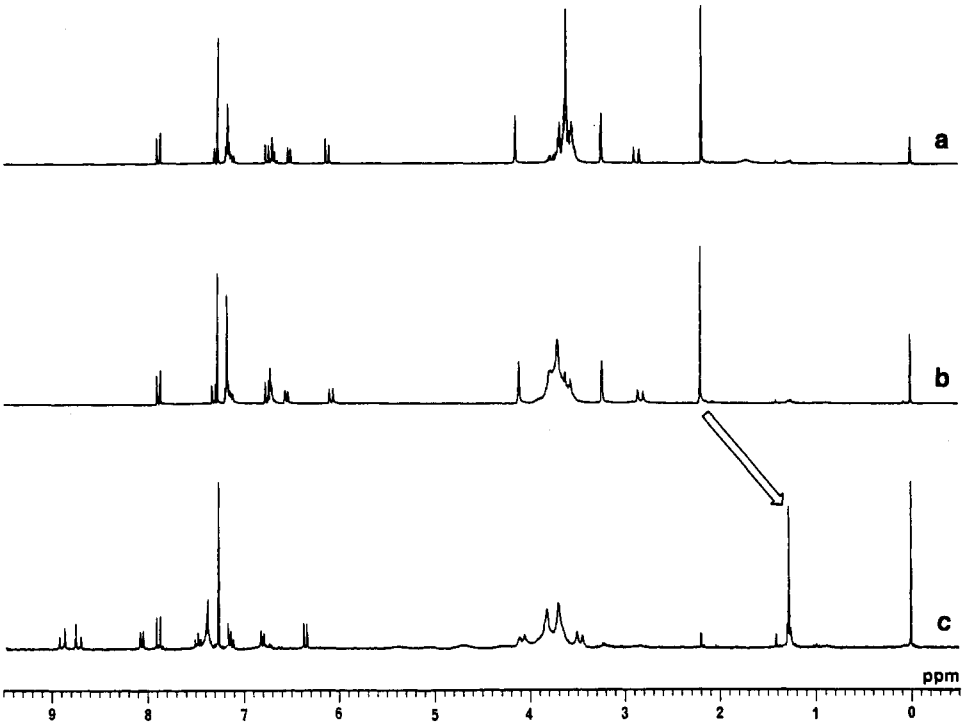

Figure 2. ^1H NMR spectra (270 MHz) of **1a** in $CDCl_3$ (a) before addition of LiI, (b) almost immediately after the addition, and (c) after 20 h.

Me groups of the open colored merocyanine (**1b'**) appeared at 2.35 ppm.

In conclusion, the present work demonstrates that recognition of lithium cations causes the spirobenzopyran to isomerize to the merocyanine, which results in a proximity of the two remote sites in the molecules. In future investigations, the design of molecules which possess reacting groups and/or a second recognition site in the transmitted parts shows further development for the multi-functional artificial receptors.

On the Solvent Dependence of *cis*-Diazene Inversion[1]

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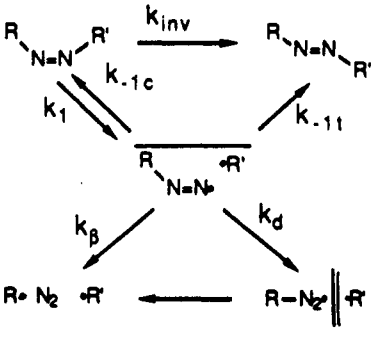
Summary: Solvent dependence of nonradical inversion rates of *cis*-diazenes cannot be due to viscosity variation because these rates are too slow. For *cis*-azoadamantane, in a variety of aromatic and nonaromatic hydrocarbons, they show a correlation with solvent internal pressure giving an approximate activation volume of +7 cm^3/mol.

We have proposed that thermal decomposition of both symmetrical and unsymmetrical *cis*-diazenes follows the mechanisms outlined in Scheme I based on the pressure[1,3] and solvent[4] dependences of their decomposition rates. Pressure retards the rates of both deazatization and isomerization, and the resulting positive activation volumes are consistent with one-bond scission deazatization (k_1) and isomerization by inversion (k_{inv}).[5] The deazatization rates

Scheme I



(1) High Pressure Studies. 29. Part 28: Neuman, R. C., Jr.; Berge, C. T.; Binegar, G. Al.; Adam, W.; Nishizawa, Y. *J. Org. Chem.* **1990**, *55*, 4564.

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(3) Neuman, R. C., Jr.; Binegar, G. Al. *J. Am. Chem. Soc.* **1983**, *105*, 134.

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(5) k(N) and k(I) are observed rate constants for deazatization and isomerization, respectively; k_1 and k_{inv} are the specific rate constants shown in Scheme I.

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Table I. Solvent Dependence of the Isomerization Rate Constant of *cis*-Azoadamantane

solvent	viscosity[a] (cp)	(viscosity)$^{0.5}$	P_i,[b] (atm)	k(I)[c,d] ($s^{-1} \times 10^4$)	ln k(I)
hexane	0.277	0.526	2358	2.60 (0.51)	0.957
octane	0.477	0.691	2626	2.38 (0.12)	0.868
nonane	0.615	0.784	2725	2.24 (0.02)	0.808
decane	0.791	0.890	2766	2.13 (0.07)	0.756
2,5-dimethylhexane	0.426	0.652	2486	2.51 (0.03)	0.921
2,2,4-trimethylpentane	0.444	0.666	2325	2.37 (0.07)	0.864
methylcyclohexane	0.627	0.792	2927	2.35 (0.06)	0.855
toluene	0.519	0.720	3501	1.73 (0.05)	0.548
ethylbenzene	0.589	0.768	3477	1.87 (0.06)	0.627
cumene	0.693	0.832	3427	1.91 (0.06)	0.649

[a] Determined at 30 °C. [b] Values of internal pressure (P_i) at 20 °C are taken from ref 13. [c] Measured at 20 °C. Numbers in parentheses represent the deviation arising from 3 to 4 determinations of the rate constant.

also decrease with increasing solvent viscosity as expected with one-bond scission.[4]

Similarly, isomerization rates appear to decrease as solvent viscosity increases for all but one of these *cis*-diazenes, and we suggested that this agreed with the inversion mechanism.[4] Recently, this interpretation of the isomerization data was questioned by Perrin.[6] He pointed out that viscosity should alter the rates of dynamic processes such as diffusion, intramolecular rotation, and inversion that are *fast*, but the isomerization/inversion processes which correspond to k_{inv} for *cis*-diazenes are slow with typical values of 10^{-4}–10^{-5} s^{-1}. This led us to search for another solvent parameter consistent with the observed solvent dependence.

We considered that separative diffusion of geminate radicals might be an important component of the isomerization mechanism as we believe it to be for the dezatization mechanism. However, the expected viscosity dependence in such a case might paradoxically be an *increase* in k(I) with increasing viscosity.[4] In addition, other data[7] support nonradical inversion (k_{inv}) as the primary isomerization mechanism for *cis*-diazenes which show the apparent decrease in k(I) with increasing solvent viscosity.[4] This led us to reexamine the solvent parameter *internal pressure* (P_i) which had been of interest to us a number of years ago.[8]

At that time, it had been proposed by *others* that atmospheric pressure rate constants and P_i values in different solvents[8] could be used, in place of data from external pressure variation experiments in a single solvent,[9] to obtain activation volumes for chemical reactions.[10] Internal pressure reflects the balance between attractive and repulsive forces in solvents and is a measure of the energy required to increase the volume of a solvent.[11] It had been argued that reactions with positive activation volumes could be slowed by solvents with high internal pressure and vice versa.

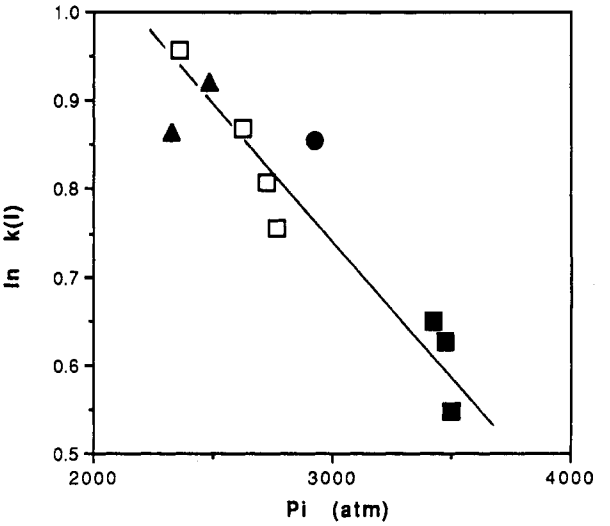

Figure 1. ln k(I) vs internal pressure (P_i).

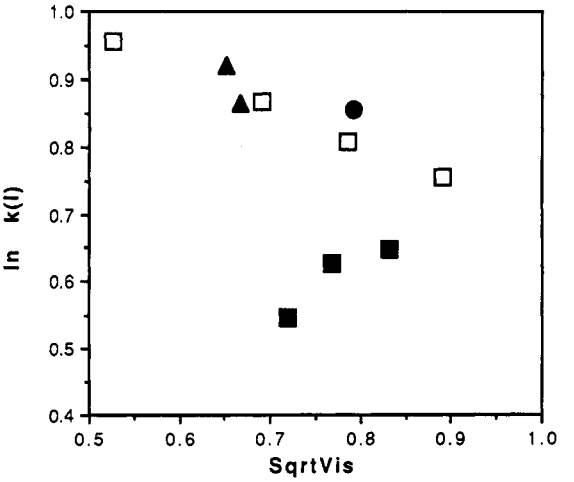

Figure 2. ln k(I) vs the square root of viscosity.

(6) (a) Perrin, C. Comments made in response to a presentation[6b] of data obtained by H. J. Gunderson.[2] (b) Neuman, R. C., Jr.; Gunderson, H. J. Pacific Conference on Chemistry and Spectroscopy, San Francisco, CA, Nov. 1, 1990.

(7) Schmittel, M.; Rüchardt, C. *J. Am. Chem. Soc.* **1987**, *109*, 2750.

(8) Neuman, R. C., Jr. *J. Org. Chem.* **1972**, *37*, 495.

(9) For reviews of pressure effects on chemical reactions see: (a) Isaacs, N. S. *Liquid Phase High Pressure Chemistry*; John Wiley & Sons: Chichester, U. K., 1981. (b) le Noble, W. J. *Progr. Phys. Org. Chem.* **1967**, *5*, 207. (c) Neuman, R. C., Jr. *Acc. Chem. Res.* **1972**, *5*, 381.

(10) Activation volumes (ΔV^*) reflect the difference in partial molar volume between the transition state and reactant(s) and can be obtained from the relationship $\partial \ln k/\partial P = -\Delta V^*/RT$.

(11) Background literature references on internal pressure are given in ref 13 of our earlier paper[8] dealing with this topic.

We concluded that meaningful activation volumes could *not* generally be obtained from rate correlations with P_i using comparable rate data from pressure experiments and solvent variation studies.[8] Although a qualitative correlation has been documented for a nonpolar rearrangement in the gas phase and a nonpolar solvent,[9b] internal pressure has frequently been misused as a correlator of reaction rates.[12]

Nonetheless, we now report that inversion rate constants (Table I), newly obtained by us for isomerization of *cis*-azoadamantane (R = R′ = 1-adamantyl) in a variety of nonpolar hydrocarbons *and* aromatic hydrocarbons,[2] which do *not* show a consistent correlation with solvent viscosity, do show a linear correlation with P_i values[13] (Figure 1). Moreover, we were startled to find that the resulting apparent "activation volume" of +7 cm^3/mol is the same within experimental error as that obtained by us several years earlier using the solvent hexane and externally applied pressure.[1,3] For comparison, a solvent viscosity plot of ln k(I) for these same data points is shown in Figure 2.[14]

As a result of this observation we will reexamine other data, which allow comparisons between activation volumes determined conventionally and calculated from P_i correlations, which we accumulated after our negative conclusions[8] about internal pressure as a rate correlator. If any correlations are obtained, we believe that they will be seen in sets of data for nonpolar reactions in nonpolar solvents where the range of solvent types is narrow. Previously, we attempted to include both polar and nonpolar solvents in a single correlation.

Acknowledgment. Financial support by the National Science Foundation and the UCR Research Committee is gratefully acknowledged.

(12) A recent literature example of the hazards of using the concept of internal pressure to qualitatively explain a solvent effect on rates is the proposal by P. A. Grieco et al. (*J. Am. Chem. Soc.* **1990**, *112*, 4595) and its refutation by M. A. Forman and W. P. Dailey (*J. Am. Chem. Soc.* **1991**, *113*, 2761). The authors thank Professor W. J. le Noble for reminding us of the easy pitfalls that can be encountered in attempting to use this parameter.

(13) The P_i values used are those reported by: Allen, G.; Gee, G.; Wilson, G. H. *Polymer* **1960**, *1*, 456.

(14) Several additional k(I) values[2] using solvents for which internal pressure values are not available are not included in Figure 2.

Siloxanes: Versatile Templates for Acyclic Stereocontrol. Synthesis of the C27–C33 Segment of Rapamycin

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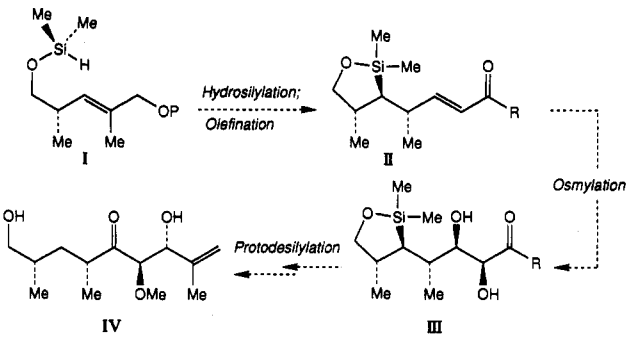
Summary: Five-membered siloxane rings may be employed to relay asymmetry along an acyclic chain in an efficient manner. Application of this method to the synthesis of the C27–C33 segment of the immunosuppressant rapamycin is reported.

The discovery of immunosuppressants FK-506[1] and rapamycin[2] has spawned a great deal of interest in these natural products both as synthesis targets[3] and with regard to the mechanism of their biological function.[4] As part of a program aimed at the total synthesis of rapamycin, we have examined the utility of cyclic siloxanes for the control and relay of asymmetry along an acyclic chain. We report herein an efficient synthesis of the C27–C33 portion of rapamycin, a segment which contains the C28–C30 anti aldol linkage.

Scheme I



Unsaturated siloxane II, formed by the Pt-catalyzed hydrosilylation of I (Scheme I), is the key intermediate in our synthesis scheme.[5] The stereogenic center α to the alkene should differentiate the diastereotopic faces of the neighboring unsaturation site. Therefore, the siloxane ring might be retained and used to relay asymmetry along the acyclic chain (I → II → III, 1,5 induction) before its re-

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